

## NATION

*A Nobel Laureate  
Gives a Boost to the AIDS  
Vaccine Program*

# A Shot in the Arm

BY MARK SCHOOFS

**E**uphoria over new AIDS therapies has incited the media to speculate about the end of the epidemic. But scientists universally believe that the only way to truly stop AIDS is by vaccinating people against HIV. To that end, the National Institutes of Health signaled a major new commitment to developing an AIDS vaccine by naming Nobel laureate David Baltimore last week to reinvigorate their foundering research program. Baltimore will chair a top-caliber scientific committee that will set priorities and coordinate the efforts of the various institutes that make up the NIH.

In a rare show of unity, scientists, industry leaders, and activists all praised the appointment of Baltimore. They point to his scientific genius as well as his stubborn and compelling character. Merck's Maurice Hilleman, who has developed more vaccines than anyone in history, summed up the prevailing view: "The government is lucky to have him."

Among Baltimore's numerous scientific achievements is the discovery of reverse transcriptase, an enzyme that is essential for HIV—and all retroviruses—to function. In the field of retrovirology, this is equivalent to discovering that the earth revolves around the sun. Baltimore proved his personal mettle when a researcher in his lab was accused of falsifying data. Baltimore staunchly defended the researcher for years—a stance which cost him the presidency of Rockefeller University—but he was vindicated this year when a top government ethics panel found no wrongdoing.

In his new post, Baltimore will need both his brains and his fortitude. For the last decade, the effort to develop an AIDS vaccine has limped along like a neglected stepchild, attracting fewer government dollars than any major AIDS research effort. Even those meager resources have not been spent efficiently, according to a prestigious review panel established by the NIH's Office of AIDS Research (OAR).

But perhaps the most alarming barometer of vaccine research is the dearth of investment by private industry, which could churn theoretical breakthroughs into an actual vaccine. A recent report by the AIDS Vaccine Advocacy Coalition, a national group of vaccine activists, reported that just four companies "can be considered to have reasonably secure programs of any size." The main reason so few companies are working on an AIDS vaccine is simple and distressing: crucial scientific questions remain unanswered. So companies are reluctant to invest in programs that amount to shots in the dark. In short, the science just isn't there.

For example, fully four years ago, monkeys were successfully vaccinated with a strain of STV (HIV's simian cousin) from which key parts had been deleted. Such an "attenuated" HIV vaccine is widely considered too dangerous. It might cause long-term health problems such as cancer, or even reconstitute itself into a fully functional, AIDS-causing virus. So scientists hope to

find another way to elicit the same biological protection. The problem, notes Baltimore, is that "no one knows why" the simian vaccines work. As a consequence, vaccinologists don't know what immune response they should try to stimulate.

It's possible that researchers could develop a vaccine without knowing exactly how it works. A few years ago, scientists discovered that injecting a virus's raw genetic material—called "naked DNA"—into animals successfully vaccinated them. That stimulated a flurry of pharmaceutical company investment, and one such AIDS vaccine is about to enter early-stage safety trials in humans.

But it's also possible that scientists will have to develop a whole new vaccine paradigm. All current vaccines, no matter how high-tech, don't fight off a viral attack themselves. Instead, they train the immune system to rebuff the invader. But HIV attacks, and almost always overcomes, the immune system itself, suggesting that the body's natural immune response may not be good enough to fend off HIV. Scientists may have to actually improve the immune system. "I feel very humble in the face of this challenge," says Baltimore.

Baltimore may also encounter another kind of challenge. Although he is starting out with strong support, he may eventually face a power struggle. He has only been appointed chair of an "advisory" committee, so he will not have direct managerial control.

The post is "a compromise," concedes activist Mark Harrington, who sat on the OAR panel that reviewed the government's research effort and called for the position Baltimore has filled. Harrington is thrilled with Baltimore because "he's very effective and doesn't take bullshit." But he says the job description was tailored to "placate" top government scientists.

So far, the strategy seems to have worked. NIH directors Anthony Fauci, William Paul, Harold Varmus, and Richard Klausner all lobbied Baltimore to take the job, and Health and Human Services secretary Donna Shalala assured him of the Clinton administration's support. In particular, OAR director Paul is deeply committed to revitalizing the government's vaccine effort. He has raised the 1997 budget by 18 per cent and says, "My own commitment is to see that trend continue."

Momentum seems to be building behind that trend. "There is greater support for vaccines, because of the recognition that research has paid off in therapy," says Paul. If the success of protease inhibitors actually does spur vaccine research, that would be a tremendous boon. Even if the new drugs end up curing patients, they are far too expensive for the Third World, where more than 90 per cent of new HIV infections occur. And in industrialized nations, HIV might well mutate into drug-resistant strains, as tuberculosis did, making the disease more difficult to treat than ever. Baltimore, who early in his career worked with Jonas Salk on polio, draws an analogy to that disease: "We had iron lungs and many fewer people died. But when we got a vaccine, *that* was the end." ♦

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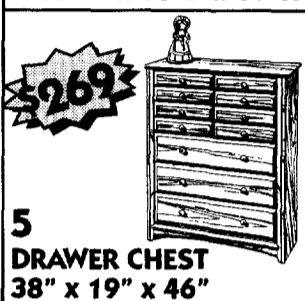


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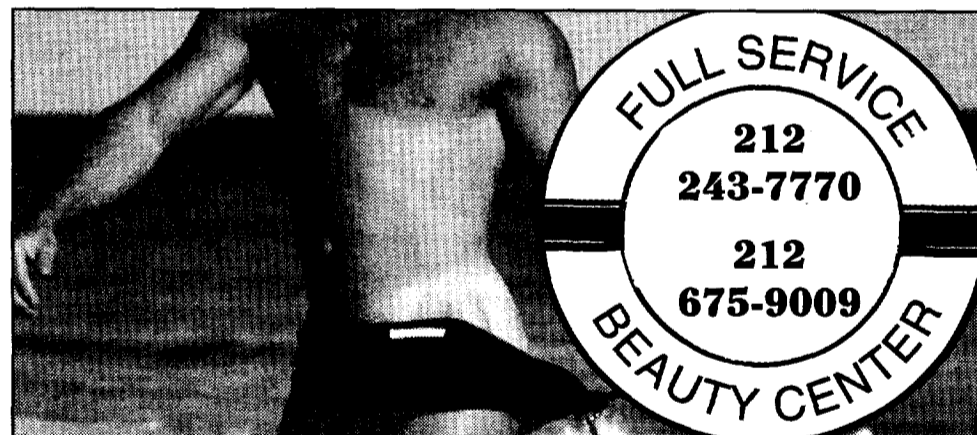
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